Historically, the rheumatic diseases have been considered chronic, disabling and incurable. Their aetiopathogenesis has been obscure. Moreover, serious molecular attempts to unravel the mystery have been ambivalent at best. Recent decades have witnessed a remarkable transformation in the approaches taken to therapeutics in rheumatology, exemplified best in the management of inflammatory arthritis. This occurred based on two fundamental paradigm shifts. First, discoveries in pathogenesis provided for the first time disease rational therapeutics, particularly biologics. Such agents have
subsequently been applied across a range of diseases and disciplines to substantial benefit, provoking the notion of mechanistically common immune-mediated diseases. Second, the application of sound strategic principles in the use of such agents is increasingly driving improvements in outcome. Herein I discuss some of the pathogenesis discovery approaches that we have employed to unravel those mechanisms that drive chronicity and co-morbidity. Such studies have evolved to support a move to defining molecular taxonomies of common inflammatory diseases, seeking in turn to develop clinically useful endotypes that can confer enriched clinical responses with reduced risk to patients. Finally, I will explore parallel translational studies in which the same principles have been applied to other common rheumatic conditions with surprising results.

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